REMARKS/ARGUMENTS

Claim rejections under 35 USC 112 first paragraph

The Patent Office rejected claims 13-18 and 23-25 under 35 USC 112 first paragraph for failing to meet the written description requirement, based on the assertion that the claims represent new matter. Applicants traverse this rejection.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. Newly added claim limitations must be supported in the specification through express, ***implicit, or inherent disclosure***. The subject matter of the claim ***need not be described literally*** (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement. Furthermore, what is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. ***If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met.*** (MPEP 2163)

Specifically, the patent office has asserted that the following terms do not have written support in the application as filed:

(a) Subcellular: The patent office asserted that "written support is provided for the image analysis of two particular subcellular components, the nucleus and cytoplasm, but not for 'subcellular' image data in general, which is broader in scope." As noted above, the written description requirement is met if one of skill in the art ***would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification.***

As an initial matter, the patent office asserted that the "Applicant points to support for 'subcellular' limitation...on page 13 (lines 22-24),..." This statement is incorrect. In their previous response, the Applicants actually pointed to page 13 (lines 22-24) as support to correct an unrelated typographical error, and not to support introduction of "subcellular" into the claims. Instead, the Applicants pointed to page 12 lines 30-31 as support for introduction of "subcellular" into the claims. This passage states the following:

"Quantification of the difference between these two ***sub-cellular*** compartments provides a measure of cytoplasm-nuclear translocation."

Furthermore, as admitted by the patent office, the specification provides support for two distinct examples of collecting image data for subcellular components, the nucleus and the cytoplasm. While this is true, the specification provides additional support for other sub-cellular compartments. For example, see page 12 (lines 1-31), 12 (lines 30-31), and page 19 (lines 1-17). On page 19 **lines -----,** the specification states:

> "***Those skilled in the art will recognize a wide variety of distinct screens that can be developed. There is a large and growing list of known biochemical and molecular processes in cells that involve translocations or reorganizations of specific components within cells.*** The signaling pathway from the cell surface to target sites within the cell involves the translocation of ***plasma membrane-associated proteins to the cytoplasm***. For example, it is known that one of the src family of protein tyrosine kinases, pp60c-src, translocates from the plasma membrane to the cytoplasm upon stimulation of fibroblasts with platelet-derived growth factor (PDGF). In contrast, some cytoplasmic components translocate from the cytoplasm to the plasma membrane upon stimulation of cells. For example, it is known that the GTP-binding proteins of the Rho family are maintained as cytoplasmic complexes with RhoGDI in resting cells, but are released and translocate to plasma membrane during cell activation. In addition, ***specific organelles, such as components of the cytoskeleton, nuclear envelope, chromatin, golgi apparatus, mitochondria, and endosomes are reorganized in response to specific stimuli.***"

Those of skill in the art are well aware that the nucleus, cytoplasm, plasma membrane, cytoskeletal components, nuclear envelope, chromatin, golgi apparatus, mitochondria, and endosomes are all sub-cellular components. Further, as explicitly stated in this section, those of skill in the art will recognize that, based on the specification, a wide variety of distinct screens can be developed, based on the methods disclosed in the application combined with the large and growing list of known biochemical and molecular processes in cells that involve translocations or reorganizations of specific components within cells. Thus, based on the teachings involving sub-cellular translocation between nucleus and cytoplasm, and the explicit teachings in the section recited above that these methods can be extended to other types of translocations and reorganizations involving components well known by those in the art to be sub-cellular, it is clear that those of skill in

the art would have understood the inventors to be in possession of the claimed invention at the time of filing.

The patent office, rather than explaining why one of skill in the art would not have understood that the inventors were in possession of the claimed invention, simply asserts that 'subcellular' "is broader in scope than nucleus and cytoplasm. However, this is not the proper test. As stated in MPEP 2163 the examiner has the initial burden of presenting evidence or reasoning to explain ***why persons skilled the art would not recognize in the original disclosure a description of the invention defined by the claims.*** This burden has not been met, and, based on all of the above, it is clear that those of skill in the art would have understood the inventors to be in possession of the claimed invention at the time of filing.

Based on all of the above, the Applicants respectfully request reconsideration and withdrawal of the rejection.

(b) Perimeter: The patent office asserted that the specification provides support for "perimeter squared area" but not "perimeter." The requirements for written description are discussed above.

As admitted by the patent office, the specification provides support for "***perimeter*** squared area." As previously argued by the Applicants, it would be understood by those of skill in the art, determining "perimeter squared area" necessarily includes determining "perimeter." The patent office asserts that "one skilled in the art could collect a perimeter squared area from the image data which does not necessarily include collecting the individual 'perimeter' measurement."

Regardless of whether this assertion is correct, it is insufficient to establish a lack of written description. Those of skill in the art would understand that "perimeter" is, at the least, implicitly and/or inherently disclosed in the specification in describing calculation of perimeter squared area, and that applicants were in possession of "calculating... perimeter". The patent office, rather than explaining why one of skill in the art would not have understood that the inventors were in possession of the claimed invention with respect to "perimeter"," simply asserts that 'perimeter "is broader in scope than perimeter squared area. However, this is not the proper test. As stated in MPEP 2163 the examiner has the initial burden of

presenting evidence or reasoning to explain ***why persons skilled the art would not recognize in the original disclosure a description of the invention defined by the claims.*** This burden has not been met, and, based on all of the above, it is clear that those of skill in the art would have understood the inventors to be in possession of the claimed invention at the time of filing.

Based on all of the above, the Applicants respectfully request reconsideration and withdrawal of the rejection.

(c) Height: The patent office asserted that the specification provides support for "height width ratio" but not "height." The requirements for written description are discussed above.

As previously admitted by the patent office, the specification provides support for "***height*** width ratio." As previously argued by the Applicant, it would be understood by those of skill in the art, determining "height width ratio" necessarily involves determining "height." The patent office asserts that "one skilled in the art could collect a height width ratio from the image data which does not necessarily include collecting the individual 'height' measurement."

Regardless of whether this assertion is correct, it is insufficient to establish a lack of written description. Those of skill in the art would understand that "height" is, at the least, implicitly and/or inherently disclosed in the specification in describing calculation of height width ratio, and that applicants were in possession of "calculating... height". The patent office, rather than explaining why one of skill in the art would not have understood that the inventors were in possession of the claimed invention with respect to "height"," simply asserts that 'height "is broader in scope than height width ratio. However, this is not the proper test. As stated in MPEP 2163 the examiner has the initial burden of presenting evidence or reasoning to explain ***why persons skilled the art would not recognize in the original disclosure a description of the invention defined by the claims.*** This burden has not been met, and, based on all of the above, it is clear that those of skill in the art would have understood the inventors to be in possession of the claimed invention at the time of filing.

Based on all of the above, the Applicants respectfully request reconsideration and withdrawal of the rejection.

(d) Ratio of fluorescent intensities: The patent office asserted that the specification provides support for "ratio of the average fluorescent intensity of the cytoplasmic mask to the average fluorescent intensity within the cell nucleus for colors 2-4" but not for "ratio of fluorescent intensities." The requirements for written description are discussed above.

As argued in the previous responses, the specification clearly provides explicit examples of using ratios of fluorescent intensities in the cytoplasm-nucleus translocation assays, as acknowledged by the Patent Office. The specification clearly provides disclosure of other translocation and reorganization assays, such as translocation between cytoplasm and plasma membrane, that can be developed based on these teachings. See, for example, page 19 lines 3-15 of the specification which states as follows:

> "Those skilled in the art will ***recognize a wide variety of distinct screens that can be developed based on the disclosure provided herein***. There is a large and growing list of known biochemical and molecular processes in cells that involve ***translocations or reorganizations of specific components within cells***. The signaling pathway from the cell surface to target sites within the cell involves the ***translocation of plasma membrane-associated proteins to the cytoplasm***. For example, it is known that one of the src family of protein tyrosine kinases, pp60c-src (Walker et al (1993), *J. Biol. Chem.* 268:19552-19558) translocates from the plasma membrane to the cytoplasm upon stimulation of fibroblasts with platelet-derived growth factor (PDGF). In contrast, some cytoplasmic components ***translocate*** from the ***cytoplasm to the plasma membrane*** upon stimulation of cells....In addition, ***specific organelles***, such as components of the cytoskeleton, nuclear envelope, chromatin, golgi apparatus, mitochondria, and endosomes are ***reorganized*** in response to specific stimuli."

The Applicants argued in the previous response that it would thus be clear to those of skill in the art that the applicants had possession of other translocation assays as of the filing date of the invention, and that, as in the cytoplasm-nucleus translocation assays, ratios of fluorescent intensities could be used in these other translocation assays.

In the response, the patent office states in the current office action "Applicants cite several passages on pages 12 and 19, but these passages fail to mention ratios." As an initial matter, this is incorrect, as the patent office has already admitted support for ratios of fluorescent intensities between cytoplasm and nucleus. Furthermore, the disclosure from page 19 recited above specifically states that "Those skilled in the art will ***recognize a wide variety of distinct screens that can be developed based on the disclosure provided herein."*** Those of skill in the art would understand that this necessarily includes the determination of ratios of fluorescent intensities between organelles as exemplified by the disclosure on cytoplasm-nuclear translocation assays on page 12 of the disclosure. The applicants go on to list another exemplary translocation assay on page 19, that between cytoplasm and plasma membrane, as well as reorganizations involving components of the cytoskeleton, nuclear envelope, chromatin, golgi apparatus, mitochondria, and endosomes. This clearly meets the written description requirements of 35 USC §112 first paragraph.

The patent office does not present evidence or reasoning to explain why persons skilled in the art would not recognize that inventors were in possession of the invention at the time the application was filed, instead simply asserting that "ratios of fluorescent intensities" is broader than the ratios as specifically described in the nucleus-cytoplasm translocation example on page 12. However, as noted above, the Applicants explicitly that those of skill in the art would recognize a wide variety of distinct screens that can be developed based on the disclosure provided herein, and then proceeded to describe a number of such further examples. Thus, it is clear that those of skill in the art would recognize that the Applicants were in possession of the claimed invention at the time of filing the application, thus the Applicants respectfully request reconsideration and withdrawal of the rejection.

(e) Difference in fluorescent intensities: The patent office asserted that the specification provides support for "the difference of the average fluorescent intensity of the cytoplasmic mask and the average fluorescent intensity within the cell nucleus for colors 2-4" but not for "differences in fluorescent intensities." The requirements for written description are discussed above.

As argued in the previous responses, the specification clearly provides explicit examples of using differences in fluorescent intensities in the cytoplasm-nucleus translocation

assays, as acknowledged by the Patent Office. The specification clearly provides disclosure of other translocation and reorganization assays, such as translocation between cytoplasm and plasma membrane, that can be developed based on these teachings. See, for example, page 19 lines 3-15 of the specification which states as follows:

> "Those skilled in the art will ***recognize a wide variety of distinct screens that can be developed based on the disclosure provided herein***. There is a large and growing list of known biochemical and molecular processes in cells that involve ***translocations or reorganizations of specific components within cells***. The signaling pathway from the cell surface to target sites within the cell involves the ***translocation of plasma membrane-associated proteins to the cytoplasm***. For example, it is known that one of the src family of protein tyrosine kinases, pp60c-src (Walker et al (1993), *J. Biol. Chem.* 268:19552-19558) translocates from the plasma membrane to the cytoplasm upon stimulation of fibroblasts with platelet-derived growth factor (PDGF). In contrast, some cytoplasmic components ***translocate*** from the ***cytoplasm to the plasma membrane*** upon stimulation of cells....In addition, ***specific organelles***, such as components of the cytoskeleton, nuclear envelope, chromatin, golgi apparatus, mitochondria, and endosomes are ***reorganized*** in response to specific stimuli."

The Applicants argued in the previous response that it would thus be clear to those of skill in the art that the applicants had possession of other translocation assays as of the filing date of the invention, and that, as in the cytoplasm-nucleus translocation assays, differences in fluorescent intensities could be used in these other translocation assays.

In the response, the patent office states in the current office action "Applicants cite several passages on pages 12 and 19, but these passages fail to mention differences." As an initial matter, this is incorrect, as the patent office has already admitted support for differences of fluorescent intensities between cytoplasm and nucleus. Furthermore, the disclosure from page 19 recited above specifically states that "Those skilled in the art will ***recognize a wide variety of distinct screens that can be developed based on the disclosure provided herein."*** Those of skill in the art would understand that this necessarily includes the determination of differences in fluorescent intensities between organelles as exemplified by the disclosure on cytoplasm-nuclear translocation assays on page 12 of the disclosure. The applicants go on to list another exemplary translocation assay on page 19, that between cytoplasm and plasma membrane, as well as

reorganizations involving components of the cytoskeleton, nuclear envelope, chromatin, golgi apparatus, mitochondria, and endosomes. This clearly meets the written description requirements of 35 USC §112 first paragraph.

The patent office does not present evidence or reasoning to explain why persons skilled in the art would not recognize that inventors were in possession of the invention at the time the application was filed, instead simply asserting that "differences in fluorescent intensities" is broader than the differences as specifically described in the nucleus-cytoplasm translocation example on page 12. However, as noted above, the Applicants explicitly that those of skill in the art would recognize a wide variety of distinct screens that can be developed based on the disclosure provided herein, and then proceeded to describe a number of such further examples. Thus, it is clear that those of skill in the art would recognize that the Applicants were in possession of the claimed invention at the time of filing the application, thus the Applicants respectfully request reconsideration and withdrawal of the rejection.

Claim rejections based on 35 USC §102(e)

The Patent Office rejected claims 13-18 and 23-25 under 35 USC 102(e)(2) over Nova et al. (US Pat. No. 5,961,923). The Applicants traverse this rejection.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. ***"To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient."*** (MPEP Section 2112, IV)

Presently pending claim 13 recites as follows:

A method for acquisition, storage, and retrieval of cell screening data on a computer system, comprising the steps of :

a) providing a plate containing wells, wherein the wells comprise cells;

b) storing input parameters used for screening of the plate in a computer system database;

c) repeating steps (i)-(ix) for a desired number of wells:

i) selecting an individual well on the plate,

ii) collecting **subcellular image data** from the cells in the well,

iii) storing the **subcellular image data** in the computer system database,

iv) collecting **feature data** from the **subcellular image data**,

v) storing the feature data in the computer system database,

vi) calculating well summary data using the **subcellular image data** and the feature data collected from the well;

vii) storing the well summary data in the computer system database;

viii) calculating plate summary data using the well summary data from the computer system database; and

ix) storing the plate summary data in the computer system database;

wherein the subcellular image data, the feature data, the well summary data, and the plate summary data can be retrieved from the computer system database.

Nova does not teach or suggest collecting **subcellular image data** from individual cells in the wells, nor, as a result, any further steps involving image data, as recited in the presently pending claims.

The patent office cites column 51 line 61 to column 52 line 9 and lines 27-60 to support the assertion that Nova teaches image acquisition to monitor edges and peak signals, as well as determining the average intensity of each cell. However, the recited section (column 51 line 61 to column 52 line 9) teaches generating a "snap-shot" of the optical memory device. This does not expressly refer to generating **subcellular** image data from cells in wells, nor does the section inherently anticipate generating **subcellular** image data from cells in wells (ie: it is not *necessarily present*). Furthermore, column 52 lines 27-60 (and corresponding Figure 31) involve determining edges and peaks for the ***symbol*** (see column 52 lines 45, 48, and 57). As noted in column 22 line 65-67, symbology refers to the

code, such as a bar code, that is engraved or imprinted on the optical memory device. Clearly, this does not expressly refer to generating **subcellular image data** from cells in wells, nor does the section inherently anticipate generating image data from cells in wells (ie: it is not *necessarily present*).

The patent office asserts that Nova "disclose using fluorophores or other luminescent moieties, labeling molecules and biological particles, tagging molecules (abstract),...", and thus anticipate the collecting of subcellular image data. However, Nova uses these fluorophores and molecules in total "to produce lumenescing matrices with memories" (abstract), which Nova teaches are "combinations...of matrix materials (abstract)" that can be encoded with an "optically readable code" (abstract). These codes provide for "information and data storage" for "tracking and identification" (column 2 lines 49-52). Thus Nova teaches using the total molecular landscape in combination with matrices to produce combinatorial libraries for the purpose of identification and tracking. As a result, Nova does not teach or suggest, for example, any of the following limitations of claim 13:

-collecting **subcellular image data** from the cells in the well,
-storing the **subcellular image data** in the computer system database,
-collecting **feature data** from the **subcellular image data**,
-storing the feature data (which is from the **subcellular image data**) in the computer system database,
-calculating well summary data **using the subcellular image data and the feature data** collected from the well;
-storing the well summary data (calculated from the **subcellular image data**) in the computer system database;
-calculating plate summary data using the well summary data (which is calculated from the **subcellular image data**) from the computer system database;
-storing the plate summary data (calculated from the well summary data which is calculated from the **subcellular image data**) in the computer system database; and
-wherein the **subcellular image data**, the feature data, the well summary data, and the plate summary data can be retrieved from the computer system database.

Thus, the Nova reference clearly is not a proper anticipatory reference for claim 13, or for any of the claims dependent on claim 13, which recite further limitations. Based on all of the above, the applicants respectfully request reconsideration and withdrawal of this rejection.

If there are any questions or comments regarding this Response, the Patent Office is encouraged to contact the undersigned attorney as indicated below.

Respectfully submitted,

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